(FILE 'HOME' ENTERED AT 12:58:38 ON 29 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 12:58:50 ON 29 OCT 2002

L1 0 S (ICOS OR JTT? OR AILIM OR 8F4 OR F23 OR C389? OR H4) AND (CO!

L2 436 S ICOS

L3 312 S (ICOS OR JTT? OR AILIM OR 8F4 OR F23 OR C389? OR H4) AND (CD2

L4 26 S L3 AND (GRAFT OR TRANSPLANT? OR GVHD)

L5 16 DUP REM L4 (10 DUPLICATES REMOVED)

L6 26 S L3 AND PY<1999

L7 13 DUP REM L6 (13 DUPLICATES REMOVED)

L8 12 S L7 NOT L5

L5 ANSWER 9 OF 16 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001372860 MEDLINE
DOCUMENT NUMBER: 21322742 PubMed ID: 11429542
TITLE: Importance of **ICOS**-B7RP-1 costimulation in acute and chronic allograft rejection.
COMMENT: Comment in: Nat Immunol. 2001 Jul;2(7):573-4
AUTHOR: Ozkaynak E; Gao W; Shemmeri N; Wang C; Gutierrez-Ramos J C;
Amaral J; Qin S; Rottman J B; Coyle A J; Hancock W W
CORPORATE SOURCE: Millennium Pharmaceuticals, Inc., 75 Sidney Street, Cambridge, MA 02139, USA.
CONTRACT NUMBER: AI40152 (NIAID)
SOURCE: Nat Immunol, (2001 Jul) 2 (7) 591-6.
Journal code: 100941354. ISSN: 1529-2908.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

AB Primary T cell activation requires **B7-CD28** and CD40-CD154 costimulation, but effector T cell functions are considered to be largely independent of these costimulatory pathways. Although blockade of costimulation with cytolytic T lymphocyte-associated antigen 4-immunoglobulin (CTLA-4-Ig) or monoclonal antibody (mAb) to CD154 prolongs allograft survival, chronic rejection follows, which suggests that additional key costimulatory pathways are active in vivo. We found that both antibody to inducible costimulator (anti-**ICOS**) and an **ICOS**-Ig fusion protein suppressed intragraft T cell activation and cytokine expression and prolonged allograft survival in a manner similar to that in **ICOS**-/- allograft recipients. The combination of anti-**ICOS** therapy and cyclosporin A led to permanent engraftment. In addition, **ICOS**-B7RP-1 costimulation was required for the development of chronic rejection after CD40-CD154 blockade. These data demonstrate a key role for the **ICOS**-B7RP-1 pathway in acute and chronic rejection and highlight the benefits of targeting this pathway in combination with the use of conventional immunosuppressive agent.

L5 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:408949 CAPLUS
DOCUMENT NUMBER: 135:370290
TITLE: Tolerance induction by costimulation blockade
AUTHOR(S): Seino, Kenichi
CORPORATE SOURCE: Clinical Medicla Surgery, Tsukuba University, Japan
SOURCE: Igaku no Ayumi (2001), 196(13), 949-952
CODEN: IGAYAY; ISSN: 0039-2359
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with refs. on costimulatory mols. and immune tolerance induction.
Transplant rejection controlled by inhibiting costimulatory signaling through **CD28**/**B7**/CTLA-4, LFA-1/ICAM-1, and CD40/CD40L systems, mechanism of costimulatory signal inhibition therapy, and costimulatory pathways of **ICOS**/B7RP-1 and LIGHT are discussed.

L5 ANSWER 7 OF 16 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001662575 MEDLINE
DOCUMENT NUMBER: 21555181 PubMed ID: 11698447
TITLE: Opposing effects of anti-activation-inducible lymphocyte-immunomodulatory molecule/inducible costimulator antibody on the development of acute versus chronic **graft**-versus-host disease.
AUTHOR: Ogawa S; Nagamatsu G; Watanabe M; Watanabe S; Hayashi T; Horita S; Nitta K; Nihei H; Tezuka K; Abe R
CORPORATE SOURCE: Division of Immunobiology, Research Institutes of Biological Sciences, Science University of Tokyo, Chiba, Japan.
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Nov 15) 167 (10) 5741-8. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011119
Last Updated on STN: 20020123
Entered Medline: 20011207

AB The functional role of inducible costimulator (**ICOS**)-mediated costimulation was examined in an in vivo model of alloantigen-driven Th1 or Th2 cytokine responses, the parent-into-F(1) model of acute or chronic **graft**-vs-host disease (**GVHD**), respectively. When the Ab specific for mouse **ICOS** was injected into chronic **GVHD** -induced mice, activation of B cells, production of autoantibody, and development of glomerulonephritis were strongly suppressed. In contrast, the same treatment enhanced donor T cell chimerism and host B cell depletion in acute **GVHD** induced host mice. Blocking of **B7**-**CD28** interaction by injection of anti-**B7**-1 and anti-**B7**-2 Abs inhibited both acute and chronic **GVHD** . These observations clearly indicate that the costimulatory signal mediated by **CD28** caused the initial allorecognition resulting in the clonal expansion of alloreactive T cells, whereas the costimulatory signal mediated by **ICOS** played a critical role in the functional differentiation and manifestation of alloreactive T cells. Furthermore, treatment with anti-**ICOS** Ab selectively suppresses Th2-dominant autoimmune disease.

L5 ANSWER 5 OF 16 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002203862 IN-PROCESS
DOCUMENT NUMBER: 21933427 PubMed ID: 11936430
TITLE: Lymphocyte costimulatory receptors in renal disease and **transplantation**.
AUTHOR: Biancone Luigi; Deambrosis Ilaria; Camussi Giovanni
CORPORATE SOURCE: Chair of Nephrology, University of Turin, Italy.
SOURCE: JOURNAL OF NEPHROLOGY, (2002 Jan-Feb) 15 (1) 7-16.
Journal code: 9012268. ISSN: 1120-3625.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020409
Last Updated on STN: 20020409

AB Cell-to-cell signal exchange during antigen presentation deeply influences the profile and extent of the immune response. Together with the TCR/MHC-mediated signal, accessory signals are provided to the T cell by the antigen-presenting cell (APC), through specific receptor-ligand interactions that represent indispensable costimulation for T-cell activation and survival. The main costimulatory pathways are the **B7** family members and the CD40-CD154 receptor-ligand pair. **B7**-1 and **B7**-2 costimulate T-cells by binding to **CD28**. Their binding is prevented by the neoexpression of CTLA4, a **CD28** homologue that can deliver a negative signal. Another **CD28**-like molecule, called **ICOS** (inducible costimulator), has been described and binds B7RP-1, a third member of the **B7** family, but not **B7**-1 and **B7**-2. The CD40-CD154 interaction works as a two way costimulatory system by triggering activation signals to both T-cell and APCs. Its importance is highlighted by the discovery that mutations of the CD154 gene are responsible for a severe human immunodeficiency. Disruption of the natural costimulatory interaction was highly effective for prevention and treatment in several experimental models of autoimmune disease and **transplant** rejection. This review focuses on the most significant advances in understanding the physiopathological events involving costimulatory molecules, and their impact on renal diseases and **transplantation**

L5 ANSWER 4 OF 16 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002239800 MEDLINE
DOCUMENT NUMBER: 21962548 PubMed ID: 11965027
TITLE: Prolonged survival in rat liver **transplantation** with mouse monoclonal antibody against an inducible costimulator (**ICOS**).
AUTHOR: Guo Lei; Li Xiao-Kang; Funeshima Naoko; Fujino Masayuki; Nagata Yuhko; Kimura Hiromitsu; Amemiya Hiroshi; Enosawa Shin; Tsuji Takashi; Harihara Yasushi; Makuuchi Masatoshi; Suzuki Seiichi
CORPORATE SOURCE: Department of Experimental Surgery and Bioengineering, National Children's Medical Research Center, Tokyo, Japan.
SOURCE: TRANSPLANTATION, (2002 Apr 15) 73 (7) 1027-32. Journal code: 0132144. ISSN: 0041-1337.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020430
Last Updated on STN: 20020509
Entered Medline: 20020508

AB BACKGROUND: An inducible costimulator (**ICOS**), a recently identified costimulatory receptor with a close structural homology to **CD28** and CTLA4, is expressed on activated T cells. Interaction with its ligand on antigen-presenting cells stimulates T-cell proliferation to produce a different spectrum of cytokine. The inhibition of **ICOS**-mediated signal transduction by an anti-**ICOS** antibody is considered to be capable of protecting against **graft** rejection in organ **transplantation**. METHODS: An anti-rat **ICOS** antibody was intravenously administered into recipients of dark Agouti-to-Lewis liver **transplantations**. The recipient lymphocytes from mesenteric lymph nodes were harvested on day 7 after **transplantation** for fluorescence-activated cell sorting analysis, and tissue specimens from the **grafts** were removed for histologic evaluation. Antigen-specific T-cell proliferation responses were assessed in vitro with anti-**ICOS** antibody. RESULTS: Monotherapy with the antibody significantly prolonged the **graft** survival time by inhibiting T-cell activation and its proliferation response. The **graft**-infiltrating cells, both CD4 and CD8 T cells, were not completely reduced even when rats were administered the antibody, whereas the expression of **ICOS** almost completely disappeared in these cells. CONCLUSIONS: T-cell activation through the **ICOS** costimulatory pathway plays an important role in **graft** rejection, and manipulating its pathway is an effective method for modulating **transplantation** immunity.

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(ICOS or JTT-? or AILIM or 8F4) and (CD28 or B7?)	27

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

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L3	(ICOS or JTT-? or AILIM or 8F4) and (CD28 or B7?)	27	L3
L2	L1	104	L2
L1	(ICOS or JTT-? or AILIM or 8F4 or H4) and (CD28 or B7?)	104	L1

END OF SEARCH HISTORY